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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,371	04/30/2001	Keld Kaltoft	KALTOFT 1	2534

1444 7590 10/21/2005

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EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/720,371	KALTOFT ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40, 60- 83 and 85-94* is/are pending in the application.

4a) Of the above claim(s) *80-83* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40, 60- 79 and 85-94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/22/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 09/01/05 is acknowledged.

Claims 40, 60- 83 and 85-94 are pending.

Claims 80-83 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

Claims 40, 60-79 and 85-94 drawn to a cytotoxic T cell line under consideration in the instant application.

2. Applicant is advised that should claim 40 be found allowable, claims 92 and 93 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

In view of the amendment, filed 09/01/05 the following rejections remain

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 37(c) of this title before the invention thereof by the applicant for patent.

4. Claims 40, 60-79 , 85-94 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 5,827,642 or by US Patent 6,316,257 for the for the same reasons set forth in the previous Office Action, mailed on 03/04/05

Applicant's arguments, filed 09/01/05 have been fully considered, but have not been found convincing.

Applicant asserts that: (i) total expansion of cytotoxic T cell which had achieved by US Patent '642 was only 30 PD. Similarly , total expansion of cytotoxic T cell which had achieved by US Patent '257 was only 27 PD. Thus none of cited references disclosed cytotoxic T cells that exceeded 40 PD as claimed in amended claims ; (ii) The immortal cytotoxic T-cell lines of the present invention have exceeded a life span of at least 40 PD because the cells have been activated by a disease-associated antigen; (iii) Delcaration by Dr. Kaltof suggested that because NK cells are present in PBMC , cytotoxic T cell taught in all three of the prior art references would not be expected to reach the presently claimed levels of at least 40 , 50 etc. PD.

Contrary to Applicant's assertion, it is noted that US Patent '642 teaches a cytotoxic human T cells that were obtained and cultured by the same method using the same culturing condition as recited in the instant Specification. US Patent '642 teaches that disease-specific antigen activated T cells were incubated in the presence of the same factors that promote T cell growth as claimed (see column 9 in particular). US Patent '642 teaches that T cells were expanded in the presence of IL-2 and anti-cD3 (see column 13 in particular). US Patent '642 teaches that cytotoxic human T cells are also capable to enter a quiescent, non-dividing phase , remain viable and then be stimulated for further expansion (see column 13, lines 35-45 in particular).

Although US Patent '642 does not explicitly teaches that the obtained cytotoxic T cells have exceeded a life-span of at least 40, 50 or 60 PD or wherein the expected life span is at least 60,100, 150 or 200 PD as claimed said functional limitation would be inherent properties of the referenced cell composition, because said cytotoxic cells were obtained and cultured by the same method using the same growth conditions as claimed. Moreover, it is noted that the Specification disclosed that only two factors in the growth medium are minimum requirement to achieve at least 40 PD or unlimited growth (see pages 3, 5, 10-12 in particular). It is noted that the same two factors are present in the growth medium taught by US Patent '642. In addition , it is noted that the referenced cytotoxic T cells have been activated by a disease-associated antigen. In the response filed on 09/01/05 Applicant acknowledge that the claimed cytotoxic T cells would exceeded a life span of at least 40 PD because the cells have been activated by a disease-associated antigen. In other words, since the activation condition in prior art references and in the instant claims are the same, the resulted cytotoxic T cells should have the same functional properties. Since the office does not have a laboratory to test the reference cytotoxic T cells is applicant's burden to show that the reference cytotoxic T cells do not have the functional properties as claimed. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

Similarly, US Patent '257 teaches a antigen-specific human cytotoxic T cell, that are obtained by rapid expansion method (see entire document, column 8 in particular). US Patent 257 teaches that culture medium comprising at least two growth factors including IL-2 ,, IL12, IL-7 (see columns 12 and 14 in particular). US Patent '257 teaches that cytotoxic human T cells are also

capable to enter a quiescent, non-dividing phase , remain viable and then be stimulated for further expansion (see column 10 in particular). It is noted that the growth condition for expansion of cytotoxic T cells of the instant specification is the same as growth condition of US Patent '257.

Although US Patent '257 does not explicitly teaches that the obtained cytotoxic T cells have exceeded a life-span of at least 40, 50 or 60 PD or wherein the expected life span is at least 60,100, 150 or 200 PD as claimed said functional limitation would be inherent properties of the referenced cell composition, because said cytotoxic cells were obtained and cultured by the same method using the same growth conditions as claimed. Moreover, it is noted that the Specification disclosed that only two factors in the growth medium are minimum requirement to achieve at least 40 PD or unlimited growth (see pages 3, 5, 10-12 in particular). It is noted that the same two factors are present in the growth medium taught by US Patent '257. In addition , it is noted that the referenced cytotoxic T cells have been activated by a disease-associated antigen. In the response filed on 09/01/05 Applicant acknowledge that the claimed cytotoxic T cells would exceeded a life span of at least 40 PD because the cells have been activated by a disease-associated antigen. In other words, since the activation condition in prior art references and in the instant claims are the same, the resulted cytotoxic T cells should have the same functional properties. Since the office does not have a laboratory to test the reference cytotoxic T cells is applicant's burden to show that the reference cytotoxic T cells do not have the functional properties as claimed. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

Claim 91 is included because the instant claims are drawn to a product (cytotoxic T-cells) and the patentability of the product does not depend on its method of production in the absence of evidence of structural difference. In re Thrope, 227 USPQ 964,966 (Fed. Cir. 1985). See MPEP 2113

With regards to the declaration submitted by the inventor Dr. Kaltoft. It is noted in said declaration, Dr. Kaltoft only expressed his position that cytotoxic T cell taught in prior art would not be expected to reach the presently claimed levels of at least 40, 50 etc., PD. Dr. Kaltoft stated that NK cells would be expected to be present in PBMC used in the prior art references and would be expected to eliminate co-cultivated disease-associated antigen-activated cytotoxic T cells. However, it is noted that there is no any objective evidences to support Dr. Kaltoft's statement that said prophetic elimination of co-cultivated disease-associated antigen-activated cytotoxic T cells actually take place in the prior art references. Moreover, it is noted that in the instant Application PBMC cells have been also used (see Examples 1 and 2 in particular).

The reference teaching anticipates the claimed invention.

5. Claims 40, 60-79 , 85-94 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 5,188,959 for the for the same reasons set forth in the previous Office Action, mailed on 03/04/05

Applicant's arguments, filed 09/01/05 have been fully considered, but have not been found convincing.

Applicant asserts that: (i) total expansion of cytotoxic T cell which had achieved by US Patent '959 was only 23-26 PD. Thus cited reference does not disclosed cytotoxic T cells that exceeded 40 PD as claimed in amended claims ; (ii) The immortal cytotoxic T-cell lines of the present invention have exceeded a life span of at least 40 PD because the cells have been activated by a disease-associated antigen; (iii) Delcaration by Dr. Kaltof suggested that because NK cells are present in PBMC , cytotoxic T cell taught in all three of the prior art references would not be expected to reach the presently claimed levels of at least 40 , 50 etc. PD.

Contrary to Applicant's assertion, it is noted that US Patent '952 teaches a cytotoxic human T cells that were obtained and cultured by the same method using the same culturing condition as recited in the instant Specification. US Patent '952 teaches that disease-specific antigen activated T cells were incubated in the presence of the same factors that promote T cell growth i.e. Il-2 and Il-4 and additional factors such as lectin or an antibody to Cd3 as claimed (see columns 8, 9 and 18 in particular) . Although US Patent '952 does not explicitly teaches that the obtained cytotoxic T cells have exceeded a life-span of at least 40, 50 or 60 PD or wherein the expected life span is at least 60,100, 150 or 200 PD as claimed said functional limitation would be inherent properties of the referenced cell composition, because said cytotoxic cells were obtained and cultured by the same method using the same growth conditions as claimed. Moreover, it is noted that the Specification disclosed that only two factors in the growth medium are minimum requirement to achieve at least 40 PD or unlimited growth (see pages 3, 5, 10-12 in particular). It is noted that the same two factors are present in the growth medium taught by US Patent '959. . In addition , it is noted that the referenced cytotoxic T cells have been activated by a disease-associated antigen. In the response filed on 09/01/05 Applicant acknowledge that the claimed cytotoxic T cells would exceeded a life span of at least 40 PD because the cells have been activated by a disease-associated antigen. In other words, since the activation condition in prior art references and in the instant claims are the same, the resulted cytotoxic T cells should have the same functional properties. Since the office does not have a laboratory to test the reference cytotoxic T cells is applicant's burden to show that the reference cytotoxic T cells do not have the functional properties as claimed. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

Claim 91 is included because the instant claims are drawn to a product (cytotoxic T-cells) and the patentability of the product does not depend on its method of production in the absence of evidence of structural difference. In re Thrope, 227 USPQ 964,966 (Fed. Cir. 1985). See MPEP 2113

With regards to the declaration submitted by the inventor Dr. Kaltoft. It is noted in said declaration, Dr. Kaltoft only expressed his position that cytotoxic T cell taught in prior art would not be expected to reach the presently claimed levels of at least 40, 50 etc., PD. Dr. Kaltoft stated that NK cells would be expected to be present in PBMC used in the prior art references and would be expected to eliminate co-cultivated disease-associated antigen-activated cytotoxic T cells. However, it is noted that there is no any objective evidences to support Dr. Kaltoft's statement that said prophetic elimination of co-cultivated disease-associated antigen-activated cytotoxic T cells actually take place in the prior art references. Moreover, it is noted that in the instant Application PBMC cells have been also used (see Examples 1 and 2 in particular).

The reference teaching anticipates the claimed invention.

The following new grounds of rejection is necessitated by the amendment filed 09/01/05.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 91 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection**.

" culturing said cytotoxic T cells in the absence of PBMC feeder cells " claimed in claim 91 represent a departure from the specification and the claims as originally filed and applicant has not pointed out where the support come from. The specification and the claims as originally field only support culturing cytotoxic T cells in the presence of at least two factors which promote T cell growth.

7. No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840 The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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